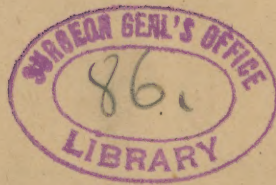


COUNCILMAN (W. T.)

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TUBERCULOSIS AS AN INFECTIOUS DISEASE.

BY WM. T. COUNCILMAN, M. D.

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Villemin, a French investigator, in 1865 first demonstrated by inoculations on rabbits and Guinea pigs, that tuberculosis is an infectious disease, capable of transmission from one animal to another. He introduced both grey miliary tubercles and cheesy pneumonic substance under the skin of the animals and found, after an interval of from ten to twenty days, tubercles in the lungs, and after a still longer period in the intestines and mesenteric glands. So striking a result led to frequent repetitions of these experiments, and the literature of the 60th years is full of the subject. The results of these first experiments were various; in general, however, the theory of Villemin encountered on all sides much opposition, both from German pathologists and from Burdon Sanderson and Fox in England. The idea came to be held that the tubercle was the result of the absorption of a thickened inflammatory exudation, and those animals, such as rabbits and Guinea pigs, in whom purulent exuda-

tions were prone to become inspissated, were most subject to tuberculosis. One of the strongest defenders of this view was Cohnheim, who, on carrying out together with Fränkel, Villemin's experiments in the Pathological Institute in Berlin, found that after the introduction of any foreign body, either a piece of paper or of cork into the abdominal cavity of rabbits and Guinea pigs, they always died of tuberculosis. Waldenberg held the view that tuberculosis could be caused by any finely divided substance being taken up by the blood.

Villemin was also not without his adherents. Especially from the experiments of Klebs it seemed that inoculation with various inflammatory products could produce foci of inflammation, but that true tuberculosis was only produced when tubercular matter was inoculated. Cohnheim and Fränkel, on repeating their experiments separately, the former in the Breslau Laboratory and the latter in his Ber-

lin dwelling, were not able to obtain their former results and were led from this to believe that the animal stalls in the Berlin Institute were thoroughly infected with the tubercular virus, and that the infection of the animals took place accidentally. Experiments were made with feeding. Aufrecht, Gerlach and others found that on feeding animals with tubercular matter tuberculosis was the result. Gerlach fed several animals with the milk of a cow that was tubercular; with one exception they all became infected. Tappeiner, and later Weichselbaum, produced tuberculosis in dogs by causing them to inhale dried tubercular sputa.

These experiments could not at all be reconciled with the theory of the absorption of an exudation, and the question seemed finally to be settled by the experiments of Cohnheim and Salomonson. In order to attain certainty in the matter they adopted the plan of introducing a small piece of caseous matter into the anterior chamber of a rabbit's eye. Here the experiment was thoroughly under their control, and any changes taking place in the tissues could be watched from day to day. When the matter inoculated was carefully cleaned it occasioned only a slight iritis at the time, which was easily controlled by atropia; the chamber remained clear and the small piece of matter could be seen attached to the iris where it remained unchanged for a period of twenty to twenty-five days. After this lapse of time small greyish nodules developed in the iris, a severe iritis was set up and the eye was lost through panophthalmitis. General infection, and a more or less severe tuberculosis of the lungs, lymph glands, etc., sometimes followed, but not in every instance. By these experiments not only the question of the inoculability of tuberculosis was settled, but what was of especial importance, it was seen that there was a definite period of incubation and that the tu-

bercles were developed primarily and without an intervening inflammation.

Let us now see how the matter stood with regard to human tuberculosis. Here the old doctrine regarding it as due to the absorption of the products of a previous inflammation played a great *role*. Buhl, whom we have to thank for so much that is good in the literature of the subject, was one of the first to call attention to the presence of a caseous focus somewhere in the body in nearly all cases of acute tuberculosis and regarded the latter as an infectious disease, or more properly speaking, a disease arising from a self-infection of the organism. For him the caseous material when once formed, no matter whether it be a caseous pneumonia or caseous lymph gland, was in itself infectious and capable on its absorption of infecting the organism with a specific disease. Taking this view of the matter, in the light of present ideas regarding infectious diseases, viz., that they are produced by a pathological agent capable of increase entering the body, there increasing and producing as a result of its presence certain specific alterations, and when transferred to another body affecting it in a similar manner, we are forced to the conclusion that the human body is in itself capable of producing such an agent, an idea which stands opposed to all our knowledge of the processes of life. The investigations of Schüppel on the so-called scrofulous lymph glands have shed much light on the matter. He always finds in these indurated caseous glands true miliary tubercles, and we are forced to the assumption that the same agent which led to the formation of tubercles here, led on its absorption to the formation of tubercles elsewhere.

When we follow the advance of tuberculosis from point to point in the body much light is thrown on its infectious nature. It is always a direct spread of the virus from one place to

another along certain definite paths. Take the most ordinary cases of tuberculosis we meet with—the advanced disease in the lungs coupled with ulcers in the larynx and ileum and a miliary tuberculosis of the liver and generally also of the spleen. How plain is here the course of the infection. The virus is taken into the lungs through the inspired air, and there the primary tubercular focus is established. From this the disease advances in the lungs, both by continuity and by independent infection of other parts of the same or of the other lung by aspiration of the sputa through the bronchi. From the lungs the virus is taken up by the lymphatics, the bronchial glands become caseous and usually the infection spreads no further in this direction. From the thorax comes the infection of the larynx, where we usually find the tubercular ulcers on the posterior larynx wall, at the spot where the sputa is apt to lie longest before being expectorated. A quantity of the sputa is always swallowed, and we have the infection of the intestinal track as shown by the ulcers in the ileum. Why the infection most generally takes place in the ileum is not accurately known; it may be that the secretions in the other parts of the digestive canal interfere with the action of the virus, or it may be that the lymphatic tissue here offers least resistance to the attack. Ulcerations in other parts of the digestive canal are by no means uncommon; only the oesophagus seems to enjoy immunity, though even here there are two or three cases reported of tubercular ulceration. From the ulcers in the ileum the disease spreads in two ways, by the lymphatics and the portal vessels; through the first we have a tuberculosis of the mesenteric glands, through the second a miliary tuberculosis of the liver where we generally find the tubercles either in the interlobular spaces or in the periphery of

the lobules. The liver acts here as a filter, retains the virus in itself and so prevents a general infection of the system; miliary tuberculosis of the liver seems to have no injurious effect on the general organism and always runs its course without symptoms.

The disease on the other hand, may begin first by an infection of the intestinal canal, and then attack gradually the mesenteric glands, the peritoneum, and in females the Fallopian tubes and the uterus. Our knowledge with regard to the infection of the whole organism with acute miliary tuberculosis as a result, has been much added to by the labors of Weigert and Ponfick. As the result of their investigations, we can say almost with an absolute degree of certainty, that in these cases we shall find a tuberculosis of the veins or of the thoracic duct. In one of these two ways the virus gets into the general circulation, and when there in sufficient quantity no organ in the body is free from its attack. Organs which are said to enjoy almost an immunity from miliary tubercle, such as the bones, the ovaries and some others, only enjoy this immunity because they are not examined with sufficient care. In three of the cases of miliary tuberculosis, I have seen, it was possible to trace the infection in this way; in one there was a large tubercular nodule in one of the pulmonary veins, in another in one of the splenic veins and in the third a caseous mass filled up the thoracic duct. That we are not able to trace definitely in such a way the source of all cases of acute miliary tuberculosis is true, but it can hardly be expected of a pathologist that he examine makro- and mikroskopically all the veins of the body. In some cases we have the infection of only a few organs through the general circulation, for instance besides the ordinary changes, a tubercular focus in the kidneys or in the brain. In such cases one must suppose that but

little of the virus got into the general circulation and was arrested here. In a few cases the epididymis or testicle and the pia mater are primarily attacked; how infection takes place in these cases we are at present unable to fully explain. For the testicle or epididymis Cohnheim suggests an infection through the act of coitus. It is true we do have tubercular affections (ulcerations) in the vagina and cervix, but when these affections exist in woman she is usually placed out of the pale of sexual pleasures. The possibility of this source of infection cannot be excluded, but it seems to me a very remote one. With regard to primary tubercular meningitis the subject is no clearer. Here the possibility has been suggested of the virus reaching the meninges through the upper nares and along the lymphatics of the olfactory nerves. Weigert asserts that in cerebro-spinal meningitis the infection takes this course, and we have generally suppuration of the ethmoid cells, but there are no cases on record where tubercular affections of this part have preceded a tubercular meningitis. Many pathologists, however, deny the existence of a primary tubercular meningitis; Prof. Chiari told me that in all his experience he had never seen a case. A number of clinical cases have been reported of primary tubercular ulceration of the larynx; these cases are rare; when, however, they do occur infection can proceed from here to the lungs and digestive tract.

For the past three years tuberculosis has been considered by most an infectious disease, and the pathogenic agent in the case of miltzbrand and other diseases having been discovered, active search began to be made for a bacterium here. Klebs, who above all others, possessed the happy faculty of finding germs wherever he sought them, was early in the field, and described an actively moving "monas tuberculosis;" Schüller and Aufrecht

soon followed, the latter describing two forms, one of which he regarded as the cause of tuberculosis and the other of phthisis. These discoveries, although causing some stir at first, were soon forgotten. They were not substantiated by other competent observers. Klebs, particularly, by his many publications over all manner of germs, publications which for the most part have never been substantiated, acquired the distrust of the profession, and his monas tuberculosis shared the same fate as his syphilis germ. This matter has been finally set at rest by a publication of Koch, in Berlin, over the ætiology of tuberculosis. His investigations here, as in all his preceding labors, were distinguished by so much care and exactness that his results, confirmed as they have been by subsequent observers, leave no room for doubt on the subject. Scarcely any publication in medicine has excited more generally the attention of the medical world; the paper has been translated and read in all tongues, and for me to give a detailed account of his work would be superfluous. Sufficient to say he finds a certain organism present in all tubercular processes, an organism definite in character, as shown not so much by its morphology as by its manner of growth. This organism he has isolated, has grown it just as the farmer grows his wheat; when one sowing comes to maturity he plants from this sowing another field (the field being represented by a test-tube filled with coagulated blood serum) and this replanting has been done in some experiments twelve times. Now having a number of animals living in the same habitation, eating the same food and being all under exactly the same conditions of life, he inoculates a certain number of them with the product of the last sowing. These become sick and die of tuberculosis; in the tubercular products are found organisms in all respects identical with

those he first started with. This he has done over and over again and always with the same result. This, I say, is proof, direct, positive, objective proof, that the organism is the cause of the disease; proof as positive as that the field of wheat is the result of the seed sown. Not only has he set at rest the question of the infectious nature of tuberculosis, but what was of especial importance, he has shown us under what conditions these germs grow, has shown us that they are true parasites growing only in the animal body, and that they usually escape from the body by means of the sputa. Since Koch's paper appeared numerous publications over the bacillus tuberculosis have followed, and in Germany all confirm fully the fact that this organism is always associated with tuberculosis, appearing both in the sputa and in the tubercles. Sternberg, in an article over the subject published in the *Medical News*, quotes an English author, Burney Yeø, who said he had never been able to find these forms, and Sternberg says that he himself has often missed them in the sputa. While working in the prosectorium of the Rudolf Hospital in Vienna, through the kindness of Prof. Chiari, and the director of the hospital, Prof. Boehm, I had ample opportunity of verifying Koch's work, both as to sputa and tissues. I examined from one ward in the hospital, with regard to the presence or absence of bacilli, thirty specimens of sputa, which were sent down to me simply with the bed numbers on the vessels. The specimens were from patients suffering from all forms of lung affection mostly tuberculosis. In three cases my report did not agree with the clinical diagnosis; the first of these was a case diagnosed as chronic bronchitis occurring in a young man of twenty-five who had rapidly lost flesh in the past five months. The sputa contained bacilli in large number. In the other two cases diagnosed as

tuberculosis I did not find them. One of these two cases afterwards died, and the only thing (in his body pointing to tuberculosis) were a few caseous and calcareous nodules in his lungs and calcified bronchial glands; what had led the clinician (an extremely careful and exact man) to make the diagnosis was the presence of bronchiectatic cavities in the right lung. A friend of mine, an army physician in Vienna, who has charge of a large military hospital there, told me he had found the bacillus in the sputa in about 95 per cent. of his tubercular patients, and in two cases had been able to differentiate between typhoid fever and acute military tuberculosis by their presence. Up to the present I know of no cases in which the urine has been examined for them in tuberculosis of the genito-urinary system, nor do I think the fæces have been investigated in cases where the ilium contains ulcers. In all probability they will be found in both these cases. The number found in the sputa is very variable; sometimes the field will be covered with them, sometimes not more than three or four will be found on a whole cover slip. The difficulties attending their recognition when so few are present, no doubt will account for the fact that some have had bad results in finding them. So far as my experience enables me to judge, their quantity in the sputa stands in no exact ratio to the extent of the disease in the lung.

One of the arguments most generally used against the infectious theory of tuberculosis is the fact that tuberculosis is essentially an inherited disease. Now the actual inheritance of tuberculosis is very questionable; some few cases have been reported of children being born with tuberculosis, but such cases are extremely rare. Even assuming this direct inheritance to be a fact does that in itself speak against infection? Few will deny that syphilis is an infectious disease, and

certainly we have inheritance here. Tuberculosis is connected with inheritance; to deny this would be to deny what is deeply rooted in the belief of all men, both the profession and the laity. Some of the German pathologists deny that inheritance has anything to do with the matter, and say that it is only seemingly so because a better opportunity is given for infection when one member of a family is tubercular. But this cannot explain it; there are too many cases known in which the children of a family all separated before any of them were affected and then living apart from one another in different parts of the country have all died of tuberculosis. To explain this we can only assume that some men are especially predisposed to tuberculosis, that their tissues are wanting in physiological resistance towards this particular virus, and that this it is that is inherited. There is no fact in medicine better established than that men differ in their susceptibility towards various diseases, and not only do individuals differ but families. There may be some difference, either chemical or other, in their tissues, a difference so subtle that we have no means of determining it, which may raise or lower the physiological resistance of the tissues towards certain diseases; this certainly in the case of tuberculosis is inherited. We must remember that the farmer must have two

factors to produce a crop, not only the seed to sow but the ground must be prepared to receive that seed.

Now, gentlemen, one word more. I have heard so often the question asked, what, after all, is the good of this discovery of Koch's, that I feel now is a good opportunity to answer it. Such questions will always be asked; in all probability when Harvey discovered the circulation of the blood many *practical* people doubted that any *practical* good could be derived from it. But I can answer. Real practical good comes from Koch's paper. One thing, it has given us in the microscopical proof of the bacillus in the sputa, an objective sign in the diagnosis of disease that is certain. I think from our present state of information on this subject that we can say while the absence of the bacillus in the sputa is no certain proof of the absence of the disease, its presence is conclusive. Its chief practical value will be found in the advance it will make in prophylaxis. It will teach us to isolate the tubercular patients in hospitals, to forbid as far as possible the marriage, and especially inter-marriage, of tubercular people, to be careful to destroy the virus that dwells in all egesta, to make laws prohibiting the sale of milk from tubercular cows, and the time may come when tuberculosis will not only be a *preventable* but a *prevented* disease.

